

What is claimed is:

1. A method for identifying a subject at risk of osteoarthritis, which comprises detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the one or more polymorphic variations are detected in a nucleotide sequence in SEQ ID NO: 1-13, or referenced in Table B, or a substantially identical sequence thereof, or a fragment of the foregoing; whereby the presence of the polymorphic variation is indicative of the subject being at risk of osteoarthritis.

2. The method of claim 1, which further comprises obtaining the nucleic acid sample from the subject.

3. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 21233000 to 21243000 of chromosome 2 in human genomic DNA.

4. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 238, 294, 295, 347, 1425, 4891, 5087, 7041, 7121, 7219, 7443, 7485, 10939, 11367, 11571, 11839, 12551, 12646, 13469, 14913, 15205, 15246, 15695, 17473, 17610, 17828, 18130, 18281, 18623, 18890, 21561, 23100, 23872, 24581, 24582, 24983, 27540, 30846, 31415, 31453, 31899, 37000, 38681, 39287, 42951, 45648, 46222, 46687, 47020, 47593, 48513, 49723, 49986, 53018, 53296, 53547, 53899, 53916, 53933, 54305, 55327, 55895, 56143, 56640, 58486, 59576, 63048, 64008, 64018, 64859, 65995, 66905, 67183, 67942, 68101, 68521, 68664, 68988, 69178, 72143, 74183, 74312, 74407, 75518, 76153, 77398, 77615, 79092, 80000, 80125, 80595, 81061, 81151, 81918, 83072, 83137, 83235, 83263, 83279, 83280, 83533, 86856, 87186, 87189, 87727, 87978, 89129, 89556, 89702, 90233, 93060, 94779, 95367, 95844, 95942, 96884, 96938, 97627, 97777, 97871, 98746 and 99663.

5. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 2 selected from the group consisting of 7219, 7485, 11839, 31899, 37000, 48513, 49986, 56640, 74407, 77398, 93060 and 97627.

6. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 102456500 to 102471500 of chromosome 2 in human genomic DNA.

7. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 225, 509, 860, 874, 939, 1483, 1798, 2189, 2215, 2282, 2340, 2963, 3369, 3481, 3564, 3653, 4860, 4941, 4975, 5321, 5346, 5541, 5633, 6007, 6317, 6378, 6382, 6426, 6479, 6641, 6703, 6705, 7963, 8525, 8526, 8598, 8624, 8883, 8980, 13578, 16135, 16141, 16642, 16931, 17004, 17009, 17010, 18713, 18853, 20783, 21335, 22180, 22268, 22285, 25378, 25906, 26015, 26475, 26798, 27042, 27649, 27827, 27873, 28122, 28202, 28232, 28240, 29546, 29748, 30054, 30646, 31149, 36912, 36936, 37184, 39064, 39343, 40868, 40917, 41113, 47343, 47806, 47911, 48009, 48621, 49245, 49247, 49299, 49302, 49514, 49626, 49791, 50010, 50294, 51482, 51556, 51855, 51956, 52155, 52448, 52458, 52511, 52607, 54049, 54224, 54567, 55052, 55857, 55941, 56120, 56349, 56727, 57232, 58806, 61181, 63808, 64526, 64865, 64928, 64966, 65080, 65690, 66228, 66982, 72511, 74170, 74264, 74333, 74502, 74741, 75321, 82558, 85366, 85469, 86485, 87687, 89463, 89660, 95718 and 95821.

8. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 3 selected from the group consisting of 2215, 3369, 16642, 20783, 52155, 55052, 55941, 74333, 74741, 85366, 85469, 87687, 89660 and 95718.

9. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 102570000 to 102583000 of chromosome 2 in human genomic DNA.

10. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 207, 6019, 6414, 7341, 10984, 12351, 13335, 16584, 16737, 23897, 24057, 25145, 25300, 26262, 26312, 26589, 27302, 27358, 27451, 27552, 30731, 32085, 32139, 33184, 42382, 42569, 44823, 45217, 45548, 45601, 45722, 45967, 47367, 47642, 48126, 49218, 49274, 49433, 49610, 51282, 51466, 53757, 53960, 54031, 54574, 55679, 56100, 56182, 59817, 60533, 60656, 72209, 72778, 74293, 77335, 78029, 78374, 78421, 78434, 79174, 79397, 79562, 79700, 79730, 79904, 79920, 79938, 79972, 80125, 80368, 83484, 85536, 85829, 86425, 88083, 88770, 90622, 90924, 91634, 92029, 95152, 95348, 96145, 96793, 97015, 97064, 97711, 97855 and 98708.

11. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 4 selected from the group consisting of 6414, 51282, 54574, 78374, 92029 and 96793.

12. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions positions 175647734 to 175655734 of chromosome 2 in human genomic DNA.

13. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 5 selected from the group consisting of 209, 5908, 7460, 7733, 7855, 7904, 8869, 9480, 13820, 15152, 17713, 17804, 18220, 19083, 19123, 19605, 20247, 20592, 21907, 23273, 23299, 23623, 23669, 23844, 24190, 24486, 24896, 25118, 30551, 30844, 30900, 30942, 31699, 32081, 35078, 36196, 36541, 38356, 45578, 49634, 49774, 51119, 51181, 51652, 54467, 55762, 55999, 57865, 66613, 68377, 69754, 72859, 76512, 76717, 77722, 80998, 82033, 89658, 89960, 94155 and 95679.

14. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 5 selected from the group consisting of 19083, 30900, 38356, 76512 and 94155.

15. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 178746000 to 178751000 of chromosome 5 in human genomic DNA.

16. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 6 selected from the group consisting of 210, 3608, 3609, 4318, 5593, 5629, 5639, 5640, 8943, 17968, 19887, 21034, 21085, , 21596, 23379, 23432, 24007, 26121, 26273, 26755, 27411, 27710, 27842, 28379, 29603, 31232, 31504, 32583, 32794, 32840, 33044, 33150, 33218, 33513, 33959, 34486, 36289, 36570, 38247, 38477, 38518, 38529, 38667, 39781, 39856, 39927, 40506, 41869, 42452, 44788, 46059, 46846, 47712, 48796, 49441, 49602, 49723, 50050, 50171, 50477, 50818, 50833, 50881, 50882, 51386, 51534, 52317, 52368, 52970, 53023, 53356, 53882, 54553, 55475, 55530, 55691, 55848, 55879, 56316, 56911, 57320, 57391, 57437, 57478, 57500, 59111, 59333, 59715, 59804, 59851, 59929, 60052, 60240, 60359, 60381, 60456, 60724, 60875, 60968, 60978, 60998, 61557, 62091, 62645, 62943, 63131, 63145, 63406, 63427, 63554, 63661, 64093, 64153, 64409, 64544, 65257, 65626, 65739, 66392, 66720, 69177, 69336, 69636, 69823, 69928, 70547, 70633, 71805, 72181, 72200, 72474, 72567, 72973, 73468, 73889, 75730, 75970, 76114, 76342, 76449, 76465, 76791, 78042, 80758, 80778, 81356, 81576, 81689, 81759, 81950, 82562, 83591, 83700, 83821, 83842, 83923, 83929, 84021, 84175, 84417, 84747, 85746, 86129, 86335, 87315, 87648, 87764, 87770, 88221, 90474, 91148, 91150, 91160, 91733, 91772, 91785, 93140, 93148, 96080, 96157, 96313, 96759, 97026, 97320, 97732, 98713,

99707, 99959, 100009, 100020, 100065, 100086, 101270, 101276, 101371, 101376, 101439, 101820, 102392, 102602, 102604, 102896, 189104, 189134 and 189205.

17. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 6 selected from the group consisting of 5640, 33150, 38247, 38529, 46846, 49723, 50050, 63427, 73889, 189104 and rs428901.

18. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 105595000 to 105615000 of chromosome 6 in human genomic DNA.

19. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 7 selected from the group consisting of 241, 801, 899, 2091, 2290, 2440, 4959, 7914, 7969, 7972, 10831, 12399, 13841, 14461, 14680, 16808, 18231, 18394, 18505, 18684, 19257, 20263, 20656, 21499, 21563, 21612, 21834, 22406, 22408, 22685, 23303, 23306, 25139, 25211, 25364, 25381, 25414, 25835, 26214, 27224, 27526, 27934, 28550, 29015, 29879, 29979, 30030, 30585, 31753, 31934, 33227, 33228, 35172, 36901, 36921, 36932, 37061, 37570, 38745, 38970, 39725, 40070, 40460, 41470, 41562, 41956, 42047, 42280, 42358, 42629, 43075, 43387, 43393, 43438, 44115, 44537, 45642, 46629, 47496, 47515, 48329, 48862, 48908, 49038, 49080, 50204, 50404, 50426, 50531, 50840, 50964, 50971, 51378, 52610, 53906, 53951, 54111, 54149, 55563, 55999, 58415, 58961, 60447, 61377, 61528, 61606, 62140, 62461, 63826, 64950, 65076, 66121, 66406, 67051, 68860, 69014, 70796, 72325, 73414, 75258, 76347, 76839, 77358, 77822, 77946, 80002, 80024, 80285, 80397, 82075, 82153, 83981, 84184, 85089, 85288, 85330, 85581, 85642, 86433, 86904, 88391, 89042, 90828, 92676, 92881, 94227, 94585, 94616, 94712, 94738, 95253, 95522, 95869 and 97856.

20. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 7 selected from the group consisting of 25414, 25835, 38970, 41470, 44115, 47496, 49038, 50204, 50840, 50964, 50971, 53906, 54149, 58415, 70796, 72325, 75258, 77822, 80002, 85288, 85581, 86904, 90828, 94616, 94712, 95869 and 97856.

21. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 27052000 to 27066000 of chromosome 12 in human genomic DNA.

22. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 8 selected from the group consisting of 230, 231, 5330, 6334, 11372, 11456, 11501, 13393, 16666, 17596, 19710, 19800, 20297, 20967, 32514, 33159, 37600, 41259, 41329, 50060, 53292, 53393, 56417, 56435, 58847, 59595, 59661, 60355, 60407, 62357, 68230, 68516, 69055, 72603, 73928, 85897 and 91554.

23. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 8 selected from the group consisting of 56435, 59595, 53292, 33159 and 41329.

24. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 71957600 to 71962600 of chromosome 15 in human genomic DNA.

25. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 10 selected from the group consisting of 213, 249, 1824, 2057, 2306, 2869, 3976, 4288, 4290, 4434, 5298, 5467, 8486, 8487, 8831, 9036, 9058, 9131, 9732, 9862, 10191, 10270, 16167, 17620, 17751, 17764, 17787, 19401, 21021, 21902, 22173, 22416, 22653, 24945, 25011, 28563, 48574, 48710, 48880, 50194, 56343, 56455, 56729, 56759, 56895, 57036, 57702, 62515, 62629, 63501, 63547, 64876, 65073, 67149, 67549, 71660, 71906 and 71911.

26. The method of claim 1, wherein a polymorphic variation is detected at position 65073 in SEQ ID NO: 10.

27. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 76221000 to 76226000 of chromosome 16 in human genomic DNA.

28. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 11 selected from the group consisting of 205, 866, 4212, 5934, 11486, 16969, 22509, 22796, 28097, 28626, 28853, 28873, 30155, 30827, 31956, 32404, 32944, 35205, 35227, 35781, 41052, 45051, 46039, 47276, 47678, 47716, 51014, 54408, 54596, 56853, 61851, 62016, 62461, 68257, 69793, 73976, 73999, 74053, 75315, 75729, 76466, 77216, 77217, 79239, 80825, 81060, 81097, 81426, 84787, 84896, 85165, 86502, 86753, 86941, 88787 and 95598.

29. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 11 selected from the group consisting of 47716 and 69793.

30. The method of claim 1, wherein the one or more polymorphic variations are detected within a region spanning chromosome positions 34828750 and 34833750 of chromosome 22 in human genomic DNA.

31. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 13 selected from the group consisting of 201, 425, 1095, 2201, 7879, 8395, 8461, 9503, 10304, 10695, 16300, 16444, 17591, 17988, 19116, 19358, 20300, 20669, 20891, 21451, 21978, 22785, 24248, 24770, 24844, 25066, 25096, 25309, 25344, 25529, 25537, 25554, 27963, 28134, 28356, 29648, 29986, 30217, 30267, 30315, 30585, 30724, 30897, 30931, 31080, 31246, 31373, 31463, 31467, 32188, 32288, 32520, 32594, 32657, 32677, 32764, 32784, 32830, 32872, 33121, 33348, 33952, 34184, 34361, 35026, 35192, 35600, 36033, 36289, 38869, 39629, 40530, 41621, 42379, 42802, 42865, 43644, 45051, 45828, 45829, 46257, 47286, 47427, 47963, 48013, 48229, 48282, 48376, 48404, 49900, 52699, 52897, 53414, 53487, 54112, 55492, 59766, 60307, 60701, 60952, 61401, 62379, 62870, 62879, 63499, 64284, 64408, 64760, 65230, 66127, , 6634, 66686, 66694, 67113, 67257, 67403, 67609, 68418, 68610, 69629, 70024, 70848, 71428, 71553, 71633, 71768, 71769, 73039, 73325, 73412, 73547, 73769, 73806, 74467, 74472, 74473, 74482, 74494, 74592, 74670, 74672, 74714, 74723, 74749, 74861, 74892, 74893, 75176, 75705, 75989, 76027, 77949, 77974, 78167, 78310, 78415, 78575, 78590, 78709, 78875, 79864, 81316, 81320, 81409, 81737, 81843, 82102, 82833, 83461, 83624, 83660, 83701, 83708, 83782, 85707, 85717, 86486, 86833, 87115, 87234, 87479, 87561, 87604, 87674, 87958, 87992, 88019, 88074, 88079, 88115, 88118, 88120, 88135, 88142, 88143, 88149, 88340, 88344, 88512, 88521, 88650, 88827, 89230, 89236, 90754, 90984, 91110, 92026, 92954, 93375, 93794, 94937, 95068, 96188, 97092 and 98812.

32. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 13 selected from the group consisting of 20300, 87958, 89236, 30267, 32657, 36289, 38869, 45051, 46257, 54112, 60307, 63499, 20891, 52699 and 71768.

33. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in Table B.

34. The method of claim 1, wherein the one or more polymorphic variations are detected at one or more positions in linkage disequilibrium with one or more positions in claim 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 or 33.

35. The method of claim 1, wherein detecting the presence or absence of the one or more polymorphic variations comprises:

hybridizing an oligonucleotide to the nucleic acid sample, wherein the oligonucleotide is complementary to a nucleotide sequence in the nucleic acid and hybridizes to a region adjacent to the polymorphic variation;

extending the oligonucleotide in the presence of one or more nucleotides, yielding extension products; and

detecting the presence or absence of a polymorphic variation in the extension products.

36. The method of claim 1, wherein the subject is a human.

37. The method of claim 36, wherein the subject is a human female.

38. The method of claim 36, wherein the subject is a human male.

39. A method for identifying a polymorphic variation associated with osteoarthritis proximal to an incident polymorphic variation associated with osteoarthritis, which comprises:

identifying a polymorphic variation proximal to the incident polymorphic variation associated with osteoarthritis, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation;

determining the presence or absence of an association of the proximal polymorphic variant with osteoarthritis.

40. The method of claim 39, wherein the incident polymorphic variation is at one or more positions in claim 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 or 33.

41. The method of claim 39, wherein the proximal polymorphic variation is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the incident polymorphic variation.

42. The method of claim 39, which further comprises determining whether the proximal polymorphic variation is in linkage disequilibrium with the incident polymorphic variation.

43. The method of claim 39, which further comprises identifying a second polymorphic variation proximal to the identified proximal polymorphic variation associated with osteoarthritis and determining if the second proximal polymorphic variation is associated with osteoarthritis.

44. The method of claim 43, wherein the second proximal polymorphic variant is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the proximal polymorphic variation associated with osteoarthritis.

45. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and
- (e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

wherein the nucleotide sequence comprises a polymorphic variation associated with osteoarthritis selected from the group consisting of in SEQ ID NO: 2 an adenine at position 7219, a guanine at position 7485, an adenine at position 11839, a thymine at position 31899, an adenine at position 37000, a cytosine at position 48513, a guanine at position 49986, a guanine at position 56640, a cytosine at position 74407, a guanine at position 77398, an adenine at position 93060 and an adenine at position 97627; in SEQ ID NO: 3 an adenine at position 2215, a deletion at position 3369, a deletion at position 16642, a cytosine at position 20783, a cytosine at position 52155, a cytosine at position 55052, a cytosine at position 55941, a

thymine at position 74333, an adenine at position 74741, a deletion at position 85366, a thymine at position 85469, a thymine at position 87687, an adenine at position 89660 and a cytosine at position 95718; in SEQ ID NO: 4 an adenine at position 6414, an adenine at position 51282, a cytosine at position 54574, a thymine at position 92029 and an adenine at position 96793; in SEQ ID NO: 5 a thymine at position 19083, a guanine at position 30900, an adenine at position 38356, an adenine at position 76512 and an adenine at position 94155; in SEQ ID NO: 6 a cytosine at position 5640, a cytosine at position 33150, an adenine at position 38247, a thymine at position 38529, an adenine at position 46846, a cytosine at position 49723, a cytosine at position 50050, a cytosine at position 63427, a guanine at position 73889, a thymine at position 189104, and an adenine at position rs428901; in SEQ ID NO: 7 an adenine at position 25414, a cytosine at position 25835, an adenine at position 38970, an adenine at position 41470, an adenine at position 44115, a guanine at position 47496, a cytosine at position 49038, an adenine at position 50204, a thymine at position 50840, a cytosine at position 50964, a cytosine at position 50971, an adenine at position 53906, a guanine at position 54149, a guanine at position 58415, a thymine at position 70796, a guanine at position 72325, a cytosine at position 75258, an adenine at position 77822, an adenine at position 80002, an adenine at position 85288, an adenine at position 85581, a guanine at position 86904, a guanine at position 90828, an adenine thymine adenine adenine sequence at position 94616, a cytosine at position 94712, a guanine at position 95869 and a cytosine at position 97856; in SEQ ID NO: 8 a thymine thymine repeat at position 56435, a thymine at position 59595, a cytosine at position 53292, a guanine at position 33159 and a thymine at position 41329; in SEQ ID NO: 10 a guanine at position 65073; in SEQ ID NO: 11 an adenine at position 47716 and a thymine at position 69793; in SEQ ID NO: 13 an adenine at position 20300, a thymine at position 46257, an adenine at position 89236, a guanine at position 30267, an adenine at position 32657, a cytosine at position 36289, a guanine at position 38869, a thymine at position 45051, a guanine at position 54112, an adenine at position 60307, a thymine at position 63499, a guanine at position 20891, a guanine at position 52699, and a cytosine at position 71768; and an allele associated with osteoporosis in Table B for positions rs910223, rs242392 and rs512294.

46. An oligonucleotide comprising a nucleotide sequence complementary to a portion of the nucleotide sequence of (a), (b), (c), or (d) in claim 45, wherein the 3' end of the oligonucleotide is adjacent to a polymorphic variation associated with osteoarthritis.

47. A microarray comprising an isolated nucleic acid of claim 45 linked to a solid support.

48. An isolated polypeptide encoded by the isolated nucleic acid sequence of claim 45.

49. A method for identifying a candidate therapeutic for treating osteoarthritis, which comprises:

(a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (i) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (ii) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (iv) a fragment of a nucleotide sequence of (a), (b), or (c); or

introducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and

(b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate therapeutic for treating osteoarthritis.

50. The method of claim 49, wherein the system is an animal.

51. The method of claim 49, wherein the system is a cell.

52. The method of claim 49, wherein the nucleotide sequence comprises one or more polymorphic variations associated with osteoarthritis.

53. The method of claim 52, wherein the one or more polymorphic variations associated with osteoarthritis are at one or more positions in claim 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 or 33.

54. A method for treating osteoarthritis in a subject, which comprises contacting one or more cells of a subject in need thereof with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(d) a fragment of a nucleotide sequence of (a), (b), or (c); and
(e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);
whereby contacting the one or more cells of the subject with the nucleic acid treats the osteoarthritis in the subject.

55. The method of claim 54, wherein the nucleic acid is RNA or PNA.

56. The method of claim 55, wherein the nucleic acid is duplex RNA.

57. A method for treating osteoarthritis in a subject, which comprises contacting one or more cells of a subject in need thereof with a protein, wherein the protein is encoded by a nucleotide sequence which comprises a polynucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
 - (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
 - (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
 - (d) a fragment of a nucleotide sequence of (a), (b), or (c);
- whereby contacting the one or more cells of the subject with the protein treats the osteoarthritis in the subject.

58. The method of claim 57, wherein the treatment comprises administration of an effective amount of a composition comprising an active *ADAMTS2* polypeptide or fragment thereof, wherein the polypeptide fragment is selected from the group consisting of: 252-1211, 253-1211, 254-1211, 255-1211, 256-1211, 257-1211, 258-1211, 259-1211 or 260-1211 of SEQ ID NO: 44.

59. The method of claim 58, wherein the polypeptide or fragment has biological activity.

60. A method for treating osteoarthritis in a subject, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the one or more polymorphic variation are detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

administering an osteoarthritis treatment to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

61. The method of claim 60, wherein the one or more polymorphic variations are detected at one or more positions in claim 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 or 33.

62. The method of claim 60, wherein the treatment is selected from the group consisting of administering a corticosteroid, a nonsteroidal anti-inflammatory drug (NSAID), a cyclooxygenase-2 (COX-2) inhibitor, an antibody, a glucocorticoid, hyaluronic acid, chondrotin sulfate, glucosamine or acetaminophen; prescribing a heat/cold regimen or a joint protection regimen; performing joint surgery; prescribing a weight control regimen; and combinations of the foregoing.

63. A method for detecting or preventing osteoarthritis in a subject, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;

(d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

administering an osteoarthritis prevention or detection procedure to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

64. The method of claim 63, wherein the one or more polymorphic variations are detected at one or more positions in claim 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 or 33.

65. The method of claim 63, wherein the osteoarthritis prevention is selected from the group consisting of administering a corticosteroid, a nonsteroidal anti-inflammatory drug (NSAID), a

cyclooxygenase-2 (COX-2) inhibitor, an antibody, a glucocorticoid, hyaluronic acid, chondrotin sulfate, glucosamine or acetaminophen; prescribing a heat/cold regimen or a joint protection regimen; performing joint surgery; prescribing a weight control regimen; and combinations of the foregoing.

66. A method of targeting information for preventing or treating osteoarthritis to a subject in need thereof, which comprises:

detecting the presence or absence of one or more polymorphic variations associated with osteoarthritis in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (b) a nucleotide sequence which encodes a polypeptide encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence encoded by a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising a polymorphic variation; and

directing information for preventing or treating osteoarthritis to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

67. The method of claim 66, wherein the one or more polymorphic variations are detected at one or more positions in claim 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 or 33.

68. A composition comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and an antibody that specifically binds to a protein, polypeptide or peptide encoded by a nucleotide sequence identical to or 90% or more identical to a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B.

69. The composition of claim 68, wherein the antibody specifically binds to an epitope comprising an amino acid encoded by rs1367117, rs1041973 and rs398829.

70. A composition comprising a cell from a subject having osteoarthritis or at risk of osteoarthritis and a RNA, DNA, PNA or ribozyme molecule comprising a nucleotide sequence identical to or 90% or more identical to a portion of a nucleotide sequence in SEQ ID NO: 1-13 or referenced in Table B.

71. The composition of claim 70, wherein the RNA molecule is a short inhibitory RNA molecule.